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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,595	05/03/2002	Audrey Goddard	10466/361	2710

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EXAMINER	
WEGERT, SANDRA L	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 11/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,595	GODDARD ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 May 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/3/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

The Information Disclosure Statement, submitted on 3 July 2006, has been fully considered. It is noted that a URL in the IDS has been replaced by the domain name. The amendment of 24 August 2006 has been entered in full.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-5 are under consideration in the instant application.

Maintained/New Objections and/or Rejections

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph

Claims 1-5 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well-established utility and must undergo extensive experimentation. The basis for this rejection is set forth at p. 2-10 of the previous Office Action

(7 February 2006).

The claims are directed to antibodies made against the polypeptide of SEQ ID NO: 88 (see Specification: *PRO1270* or DNA66308-1537). Further limiting claims are presented to monoclonal antibodies, humanized antibodies, antibody fragments, labeled antibodies, and antibodies that bind "specifically" to the polypeptide. However, the specification does not disclose a function for the antibodies against SEQ ID NO: 88, in the context of the cell or organism.

Applicants' arguments in the responses submitted 3 July 2006 and 24 August 2006, as they pertain to the rejections, have been fully considered but are not deemed to be persuasive for the following reasons:

To summarize, for utility of the claimed PRO1270 antibodies, Applicants rely on the microarray data for the gene encoding the polypeptide. They argue that the results are enabling for the antibody that binds the polypeptide of SEQ ID NO: 88. They further argue that PRO1270 message is differentially expressed in cancerous lung versus control tissues, and point to the results of the expression assay (pages 140-143, Specification). The assay indicated showed a 2-fold or greater fluorescence in a Universal Control versus cancerous lung.

It is the examiner's position that the present Specification fails to disclose the physiological significance of the PRO1270 antibody or what the correlation between PRO1270 mRNA and PRO1270 polypeptide expression is, or the significance of any such correlation in lung tumors. A specific benefit does not exist in currently available form because the skilled artisan would not know if the expression of the PRO1270 polypeptide would be upregulated,

down-regulated, or unchanged in cancer. Therefore, Applicant's assertion of the overexpression of the PRO1270 gene does not impute a specific and substantial utility to the PRO1270 antibody.

Specific arguments are addressed below:

The Examiner maintains the previous argument of record, namely that mRNA levels are not necessarily predictive of protein levels, and in response to Applicants' arguments at p. 10-13 of the 24 August 2006 Response, maintains that this is true even when there is a change in the mRNA level. As discussed in prior Office Actions, comprehensive studies where significantly large numbers of transcripts and proteins were examined report that increases in mRNA and protein samples are not correlated. It is also noted that the specification of the instant application does not teach a change in mRNA level of PRO1270. The specification simply discloses a static measurement of PRO1270 mRNA in lung tumors as compared to a universal control. There are no teachings in the specification as to the differential expression of PRO1270 mRNA in the progression of lung tumors in response to different treatments of hormones (for example). Therefore, the Examiner maintains that Applicants' measurements of an increase of PRO1270 mRNA does not provide a specific and substantial utility for the encoded protein or claimed antibody.

The specification of the instant application has only disclosed that the PRO1270 polynucleotide is underexpressed in lung tumors. The specification does not indicate that the PRO1270 polypeptide has been underexpressed in the lung tumor samples tested. Given the asserted decrease in PRO1270 expression, and the evidence provided by the current literature, it is clear that one skilled in the art would not assume that an decrease in mRNA expression would

correlate with significantly decreased polypeptide levels. Further research needs to be done to determine whether the purported decrease in PRO1270 cDNA supports a role for the peptide or antibody in the cancerous tissue; such a role has not been suggested by the instant disclosure. Such further research requirements make it clear that the asserted utility is not yet in currently available form, i.e., it is not substantial. This further experimentation is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. As discussed in *Brenner v. Manson*, (1966, 383 U.S. 519, 148 USPQ 689), the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and, "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Accordingly, the specification's assertions that the PRO1270 antibodies have utility in the fields of cancer diagnostics is not substantial.

Applicants discuss the declaration under 37 CFR § 1.132 by Scott to make the argument that it is generally agreed that there is a correlation between mRNA levels and expression levels of the translated proteins (Remarks, p. 2, 24 August 2006). Similar arguments are addressed below.

It is noted that at pages 5-7 of the Remarks of 3 July 2006, Applicants cite pertinent case law reviewing the legal standard of utility and the Utility Examination Guidelines. The examiner takes no issue with Applicant's general comments regarding the legal standard for utility.

At p. 8 of the Remarks, Applicants maintain that the specification at, for example, Example 18, provides sufficient disclosure to establish a specific, substantial and credible utility

for the PRO1270 polypeptides and antibodies. Applicants argue that Example 18 discloses that PRO1270 is significantly underexpressed in human lung tumor tissues as compared to a non-cancerous human tissue control. Applicants argue that the utilities of PRO1270 antibodies include the use as a diagnostic tool.

Applicants' arguments have been fully considered but are not found to be persuasive. Specifically, in the instant case, the specification indicates underexpression of PRO1270 mRNA in lung tumor tissue (the numerical change is not known). However, the specification fails to precisely disclose any correlation between the reported underexpression of PRO1270 mRNA and PRO1270 protein expression, and more importantly, to what extent PRO1270 mRNA is reliably underexpressed in a particular tumor sample, such as lung, such that the PRO1270 polypeptide encoded thereby could be used as a diagnostic marker for lung tumors. There is no evidence regarding whether or not PRO1270 polypeptide levels are underexpressed in lung tumors.

As discussed in the previous Office Action, a utility of being a diagnostic target for lung tumors is a utility that requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use. This is not a substantial utility. In Example 18, Applicants teach that PRO1270 was underexpressed in lung tumors as compared to the universal normal control. The utility of the universal normal control has never been questioned. Rather, one of the issues is that there is no guidance in the specification as to how high the levels of underexpression are. Neither the specification nor the declarations provide any evidence that indicates what the differences were. For example, if a clinician took a lung tissue sample from a patient with suspected lung cancer, what is the likelihood that when compared with normal

tissue, the level of PRO1270 from the patient would be higher? How many samples would be needed? What sensitivity would be needed? Would the normal tissue have to be a pooled sample or could it be from a single individual? Applicant has provided no indication of the nature or number of samples that were used. The only thing Applicants teach is that PRO1270 was "less highly expressed", and this does not enable the skilled artisan to differentiate amongst expression levels in order to diagnose any diseases. As was stated previously, the literature cautions researchers from drawing conclusions based on small changes in transcript expression levels between normal and cancerous tissue. Without more specifics about necessary sample size, expression level range for normal and tumor tissues, the specification has not provided the invention in a form readily usable by the skilled artisan such that significant further experimentation is unnecessary.

Specifically, although the "universal control" of the instant application is derived from tissues of epithelial origin (p. 135, line 1 of the instant specification), there is no teaching in the specification that any epithelial samples were derived from lung. This issue is of importance because the specification asserts that the PRO1270 nucleic acid is underexpressed in lung tumor cells. It is not clear as to why the tumor tissues in Example 18 are not compared to single organ control samples. Additionally, the state of the art discloses that a normal standard is not so easy to define and, furthermore, gene expression in normal tissue is dependent upon several factors involving patient and sample variation (King et al., 2006, J. Am. Med. Assoc., 286: 2280-2288, p. 2281, col 1, 2nd full paragraph). One complication encountered with microarray expression profiles is that any given tissue is composed of many different cell types. For example, King et al. teaches that:

"a simple punch biopsy of the skin may contain keratinocytes, melanocytes, Langerhans cells, Merkel cells, adipocytes, smooth muscle cells of erector pili, striated muscle cells of the panniculus carnosus, blood cells including immune system cells, and cellular elements of blood vessels, nerves, hair follicles, sebaceous glands, and sweat glands. Moreover, cells from each of these populations will be at various stages of development and levels of activation, performing different functions and responding to disease processes or treatments in different ways and to varying extents" (p. 2282, bottom of col 2 through the top of col 3).

Thus, pooling *different* non-cancerous human epithelial tissues for a "universal control" introduces variability in the microarray assay. Utilization of incorrect tissue for comparison (with the absence of, or diminished expression of a gene in a particular tissue) would artificially increase or decrease the magnitude of differences observed in the instant microarray. It is also noted that the specification of the instant application at p. 121 does not even indicate that the tissues used for the "universal control" were isolated from the same subject as the tumor sample subject. Again, using tumor and control samples from different subjects would introduce variability into the microarray assay, making it less comparable and accurate.

Additionally, it is well known in the art that different tissues express different genes, which is what makes the liver different from the heart and the heart different from the brain. All tissues have the same genetic makeup, but gene expression is what dictates the function of particular tissues. In the instant case, proper controls are dependent on the tissue examined since tissue specific gene expression is a natural phenomenon. An equally confounding problem of using the wrong tissue for comparison is the absence of, or *diminished* expression of a gene in a particular tissue. Accordingly, this would artificially increase or decrease the magnitude of differences observed in the instant microarray as well.

The PRO1270 gene and polypeptide of the instant application have not been associated with tumor formation or the development of cancer, nor have they been shown to be predictive

of such. The specification merely demonstrates that PRO1270 was purportedly underexpressed in cancer samples. No mutation or translocation of PRO1270 has been associated with any type of cancer versus normal tissue. It is not known whether PRO1270 is expressed in corresponding normal tissues, and what the relative levels of expression are. In the absence of any of the above information, all that the specification does is present evidence that PRO1270 mRNA is decreased in lung cancer samples and invites the artisan to determine the significance of this decrease.

In the instant case, the Specification fails to disclose the biological functions, physiological significance, or any specific and substantial utility of the claimed PRO1270 antibodies. Without such information, how can one in the skilled art use the claimed invention in a meaningful manner? See *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

Without more specifics about necessary sample size and expression level ranges for normal and tumor tissues, the instant Specification has not provided the invention in a form readily usable by the skilled artisan such that significant further experimentation is unnecessary. The importance of replication in microarray gene expression studies is also demonstrated by Lee et al. (2000, Proc. Natl. Acad., USA, 97(18): 9834-9839) who report that, "our results show that any single microarray output is subject to substantial variability" and "we recommend that at least three replicates be used in designing experiments using cDNA microarrays" (see p. 9834, second column). A single output yields numerous misclassifications, especially numerous false positives (Lee et al., bottom of p. 9838). The importance of replication in microarray gene expression studies is also important when one considers the problem of variations within

"normal" gene expression levels as reported by King et al. (JAMA, 286(18): 2280-2288, 2006). King et al. report that "a significant portion of microarray data variability for high- or medium-abundance mRNAs may simply be due to normal expression variations" and that "Several previous studies have used arbitrary 2-fold change criteria to define significant expression change. However, the 2-fold threshold has been shown to be statistically invalid even for duplicate experiments" (see p. 2284, first column).

Regarding Hu et al., Applicants indicate that among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease. At p. 10 of the Remarks, Applicants argue that Hu et al. does not show a lack of correlation between microarray data and the biological significance of cancer genes. Applicant also states that Hu et al. manipulated various aspects of the input data. Applicant urges that a paper discussing a particular type of tumor cannot be generalized as a principle governing microarray study of lung or other cancers in general. Applicants are urging an improper standard. They assert that Example 18 of the instant specification provides substantial disclosure of experimental design and data analysis to support the credibility of the microarray assay.

Applicants' arguments have been fully considered but are not found to be persuasive. The asserted utility for the claimed antibodies is based on Applicants' assertion that increased mRNA production leads to increased protein production. Hu et al. analyzed 2286 genes that showed a greater than 1-fold difference in mean expression level between lung cancer samples and normal samples in a microarray (p. 408, middle of right column) and discovered that, for

genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease. The instant specification does not disclose that PRO1270 mRNA levels are expressed at 10-fold or higher levels compared with normal, matched tissue samples. Therefore, based on Hu et al., the skilled artisan would not reasonably expect that PRO1270 protein can be used as a cancer diagnostic. Regarding Applicant's criticism of Hu et al.'s statistical analysis, Applicant is holding Hu et al. to a higher standard than their own specification, which does not provide proper statistical analysis such as reproducibility, standard error rates, etc. Regarding Applicant's criticism of Hu et al. as being limited to a specific type of lung tumor, Hu et al. is cited as one of several pieces of evidence that gene amplification in a tumor does not correlate with mRNA overproduction or protein overproduction. Applicants repeatedly try to impugn references for being drawn to different genes than PRO1270, or different types of cancers, but have provided no more "relevant", (e.g. closer to the instant fact situation) data or references. Accordingly, the record must be judged for what the cited references teach. When viewed with the evidence of record as a whole, there is no correlation between gene underexpression, mRNA levels and protein levels. In view of the totality of the evidence, including the Declarations submitted under 37 CFR 1.132 and the publications of record, the instant utility rejection is appropriate.

In the Responses of 3 July 2006 and 24 August 2006, Applicants have submitted teachings from Alberts, B. (Molecular Biology of the Cell (3rd ed 1994 and 4th ed 2002)) and

Lewin, B. (Genes VI 1997) to support the previous statements of Dr. Grimaldi (Declaration under 37 CFR § 1.132, 27 September 2004). Applicants also cite numerous references (such as Zhigang et al., Meric et al. Orntoft et al., Wang et al., Munaut et al., etc., submitted concurrently) to emphasize that those of skill in the art would not be focusing on differences in gene expression between cancer cells and normal cells if there were no correlation between gene expression and protein expression. Applicants assert that changes in mRNA level generally lead to corresponding changes in the level of expressed protein. Applicants also contend that the references and the Grimaldi Declaration establishes that the accepted understanding in the art is that there is a reasonable correlation between changes in gene expression and the level of the encoded protein.

Applicants arguments have been fully considered but are not found to be persuasive. While the examiner acknowledges the teachings of Alberts and Lewin, which disclose that initiation of transcription is the most common point for a cell to regulate the gene expression, it is not the only means of regulating gene expression. For example, Alberts also teaches that there are a number of other controls that can act later in the pathway from RNA to protein to modulate the amount of protein that is made, including translational control mechanisms and mRNA degradation control mechanisms (see Alberts 3rd ed., bottom of p. 453). Meric et al. states the following:

"The fundamental principle of molecular therapeutics in cancer is to exploit the differences in gene expression between cancer cells and normal cells. [M]ost efforts have concentrated on identifying differences in gene expression at the level or mRNA, which can be attributable to either DNA amplification or to differences in transcription."

However, Meric et al. also goes on to state that gene expression is quite complicated, and is also regulated at the level of mRNA stability, mRNA translation, and protein stability (see page 971, Introduction). Meric et al. also teaches that there are a number of translation alterations encountered in cancer, including variations in the mRNA sequence as a result of mutations, alternate splicing and transcription start sites, alternate polyadenylation sites, and alterations in the components of the translation machinery (see pages 973-974).

The Declaration of Dr. Grimaldi was previously considered by the Examiner in the Office Action of 6 December 2004. Applicant's arguments and the Grimaldi and Scott declarations have been fully considered but are not found to be persuasive. In assessing the weight to be given expert testimony, the examiner may properly consider, among other things, (1) the nature of the fact sought to be established, (2) the strength of any opposing evidence, (3) the interest of the expert in the outcome of the case, and (4) the presence or absence of factual support for the expert's opinion. See Ex parte Simpson, 61 USPQ2d 1009 (BPAI 2001), Cf. Redac Int'l. Ltd. v. Lotus Development Corp., 81 F.3d 1576, 38 USPQ2d 1665 (Fed. Cir. 1996), Paragon Podiatry Lab., Inc. v. KLM Lab., Inc., 948 F.2d 1182, 25 USPQ2d 1561, (Fed. Cir. 1993). Affidavits or declarations are provided as evidence and must set forth facts, not merely conclusions. In re Pike and Morris, 84 USPQ 235 (CCPA 1949). (1) In the instant case, the nature of the fact sought to be established is whether or not mRNA levels are predictive of protein levels. Dr. Grimaldi declares that 80% of approximately 200 instances of elevated mRNA levels were found to correlate with increased protein levels. There is no specific indication in the Grimaldi Declaration that PRO1270 mRNA was elevated and correlated with increased protein levels. (2) It is important to note that the instant specification only discloses mRNA data for PRO1270 and

does not disclose any information regarding PRO1270 protein levels. Furthermore, there is strong opposing evidence showing that mRNA levels are frequently not predictive of polypeptide levels in normal and cancerous tissues. See, e.g., Hu et al., discussed above. (3) Regarding the interest of the expert in the outcome of the case, it is noted that Dr. Grimaldi is employed by the assignee. (4) Finally, Dr. Grimaldi refers to facts; however, the data are not included in the declaration so that the examiner could independently evaluate them. For example, how many of the tumors were lung tumors? How highly amplified were the genes that correlated with increased polypeptide levels?

Firstly, all of Applicants' newly cited references measure mRNA with assays other than microarray, which is the assay utilized in Example 18 of the instant specification. Also, with the exception of Futcher et al., all of Applicant's newly cited references are directed to the analysis of single genes, or a small group of genes, and therefore do not demonstrate trends found across proteins in general. The studies cited by Applicants that examine the expression of specific genes or small numbers of genes are not found persuasive in view of comprehensive studies where significantly larger numbers of transcripts and proteins were examined and more accurately describe general trends, specifically, Haynes (80 proteins examined) and Chen (165 proteins examined) (cited previously by Examiner).

Applicants also assert that Futcher et al. (1999) conducted a study of mRNA and protein expression in yeast and report a good correlation between protein abundance, mRNA abundance, and codon bias (Response, p. 20). Applicant's arguments have been fully considered but are not found to be persuasive. Futcher et al concludes that "[t]his validates the use of mRNA abundance as a rough predictor of protein abundance, at least for relatively abundant proteins

[emphasis added]" (p. 7368, col 1). Futcher et al. also admits that Gygi et al. performed a similar study and generated similar data, but reached a different conclusion. Futcher et al. indicates that "Gygi et al. feel that mRNA abundance is a poor predictor of protein abundance" (p. 7367, col 1, 1st full paragraph).

Similar assertions are made concerning Godbout, et al (1998). Namely, Applicants assert that there are good correlations among gene copy number, transcript levels and protein levels in cancer cell lines (Response, p. 20). However, the Godbout, et al paper discusses the frequent occurrence of so-called "passenger genes," or genes that are only amplified because of their proximity with respect to amplicons, but are rarely, if ever, transcribed. They explain:

> "It is generally accepted that co-amplified genes are not over-expressed unless they provide a selective growth advantage to the cell. For example, although ERBA is closely linked to ERBB2 in lung cancer and both genes are commonly amplified in these tumors, ERBA is not underexpressed. Similarly, three genes mapping to 12q13-14 (CDK4, SAS and MDM2) are underexpressed in a high percentage of malignant gliomas showing amplification of this chromosomal region, while other genes mapping to this region (GADD153, GL1, and A2MR) are rarely underexpressed in gene-amplified malignant gliomas. The first three genes are probably the main targets of the amplification process, while the latter three genes are probably incidentally included in the amplicons" (p. 21167, right column, first full paragraph).

Thus, we see in a comprehensive study of cancer cell lines, many amplified genes are simply not transcribed. The examiner agrees with the Applicants' point about the correlation between message and protein in the DDX1 gene. The Godbout, et al paper shows that it is the rare gene indeed that is transcribed and translated, and subsequently upregulated in a causative way in cancer cells. DDX1 was shown to be an RNA helicase involved in cancer cell proliferation. However, few of the other amplified or transcribed genes that were "passengers" on the DDX1 amplicon were shown to produce protein product.

35 U.S.C. § 112, first paragraph (Enablement)

Claims 1-5 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth in the previous Office Action (7 February 2006). Applicants do not discuss Enablement of the claimed antibodies, except to say that it is related to Utility. The rejection is therefore *maintained* for reasons of record.

Conclusion

No claims are allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SLW
6 November 2006

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